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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,461	02/12/2004	Erika Hawkins	341.022US1	2264

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EXAMINER

HANLEY, SUSAN MARIE

ART UNIT	PAPER NUMBER
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1651

MAIL DATE	DELIVERY MODE
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05/01/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/777,461

Applicant(s)

HAWKINS ET AL.

Examiner

Susan Hanley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-69 is/are pending in the application.
- 4a) Of the above claim(s) 2,4,5,9-11,16-21,27-32,37,45,46,48,53 and 57-64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,6-8,12-15,22-24,33-36,38-44,47,49-52,54-56 and 65-69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 February 2004 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/13/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-42, 56 and 69; and the following specie election:

A. Quenching agent for the first or second enzyme-mediated reaction: a sequestering agent that is a nonionic detergent;

B. First enzyme-mediated luminescence reaction: *Renilla reniformis* luciferase-mediated;

C. Second enzyme-mediated luminescence reaction: *Photinus pyralis* luciferase-mediated;

in the reply filed on 1/31/07 is acknowledged. The traversal is on the ground(s) that the inventions of Groups I and II are closely related because the claims are directed to methods of assaying an enzyme-mediated luminescence reaction employ the components of the claimed kit. Applicants argue that due to the relatedness of the subject matter of at least the claims in Group I and Group II as discussed above, those Groups can be efficiently and effectively searched in a single search with no additional burden placed on the Examiner. Regarding the elections of species, Applicants argue that the requirement to elect species is traversed on the basis that the species have a disclosed relationship. The disclosed relationship for the first elected specie is that the sequestering agent, the colored compound and the substrate analog inhibitor are selective quench agents for luminescence reactions, and that the nonionic detergent, crown ether, glycol and cyclodextrin are sequestering agents. The disclosed relationship for first and second enzyme-mediated reactions is that they are all luminescence reactions.

Applicants' argument is found persuasive, in part. Groups I and II (method and kit) will be rejoined insofar as they read on the elected species. Applicants' arguments regarding the elected species are not found persuasive because an alleged "disclosed relationship" among certain species does not overcome the distinctness among the species or the considerable search burden. Regarding the sequestering agents, nonionic detergents and the sequestrants named in claim 9 (crown ethers, glycol or cyclodextrin) have distinct structures and mechanisms by which they act as sequestrants. Nonionic detergents form micelles and the compounds of claim 9 are chelators. Hence, nonionic detergents and chelators are patentably distinct and require different fields of searching in the patent and non-patent literature. The other claimed quenching agents, colored compounds and substrate analog inhibitors also have unrelated structures and inhibit luminescence by different mechanisms. The identification of a colored compound would not necessarily identify a sequestering agent or a substrate analog inhibitor. Likewise, the claimed enzymes have different structures, mechanisms, substrate specificities, co-factor requirements and inhibitors. The identification of a quenching agent for one type of enzyme-based luminescence would not necessarily identify a quenching agent for another enzyme-based luminescence systems that requires different substrates and co-factors. Furthermore, the consideration of the order of selective quenching agents also increases the complexity of the search burden.

Therefore, Groups I and II are rejoined. However, the specie elections are maintained. The elected specie for the sequestering agent is a nonionic detergent. The first enzyme-mediated luminescence reaction is *Renilla reniformis* luciferase-mediated and the second enzyme-mediated luminescence reaction is *Photinus pyralis* luciferase-mediated.

The requirement is still deemed proper and is therefore made FINAL.

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Claims 2, 4, 5, 9-11, 16-21, 27-32, 37, 45, 46, 48, 53 and 57-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/31/07.

Claims 1, 3, 6-8, 12-15, 22-24, 33-36, 38-44, 47, 49-52, 54-56 and 65-69 are presented for examination.

Drawings

Figure 5 should be designated by a legend such as --Prior Art-- because only that which is old is illustrated. See MPEP § 608.02(g). Corrected drawings in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 6-8, 12, 13, 22-24, 32-36, 38-42, 44, 49-51, 54 and 65-67 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Sherf et al. (US 5,744,320; cited in the IDS filed 9/17/04).

Sherf discloses a dual reporter assay having a selective quenching step of the first reporter. Another embodiment includes the addition of a reagent that quenches the first reporter and activates the second reporter. The first and second reporters are enzyme-mediated luminescent reactions that are distinct from one another (abstract and col. 6, lines 19-52). In the Sherf patent, claim 44 (which depends from claims 26 and 1) recites (a) initiating a first enzyme-mediated luminescence reaction can be mediated by *Renilla reniformis* luciferase; (b) quantifying the luminescence energy from the first reaction; (c) adding a quench-and-activate solution to quench the luminescence energy produced by the first reaction and simultaneously initiating the second enzyme-mediated reaction that is distinct from the first enzyme-mediated reaction wherein the luciferase is from *Photinus pyralis* (firefly); and (d) quantifying the luminescence energy produced by the *Photinus pyralis* luciferase. This disclosure meets the limitations of instant claims 1, 3, 12, 24, 33, 38-42 which are related to the general method steps. The disclosure further meets the limitations of instant claims 13 (*Renilla luciferase*); instant 22 and 23 (*Photinus pyralis* luciferase), and instant 34-36 (first reaction is mediated by a *Renilla reniformis* luciferase and second reaction is mediated by a *Photinus pyralis* luciferase, which meets the elected species). In Table 3, Sherf discloses that *Renilla* luciferase luminescence can be quenched by Tween®20 or Triton®X-100. The disclosure of Tween®20 and Triton®X-100 meets the limitations of a selective sequestering agent that is a nonionic detergent, as in instant claims 6-8. The initiator for *Renilla*

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luciferase comprises its substrate, buffer and coelentraxine (col. 15, lines 62- col. 5, lines 5). The initiator for firefly luciferase is disclosed as BLA (col. 12, lines 1-5) and the conventional firefly luciferase has been improved by adding coenzyme A to the initiator reagent to improve enzyme turnover (col. 1, lines 63-68).

The luciferase-mediated reaction is preferably quenched by reducing photon emissions from the first luciferase-mediated luminescence reaction by a factor of at least 1,000-fold (col. 9, lines 33-38), as in instant claims 40 and 42.

Sherf also discloses a kit that includes a first functional enzyme substrate for a first enzyme-mediated luminescence reaction, in a suitable first container. A second suitable container comprises a composition having a quench-and-activate reagent that selectively quenches the first enzyme reaction by a factor of at least 1,000-fold and a second and distinct functional enzyme substrate corresponding to a second distinct enzyme-mediated luminescence reaction. The kit can also include a suitable third container having a second quench reagent capable of quenching the second distinct enzyme-mediated reaction. This disclosure meet the limitations of instant claims 44, 49-51, 54, and 65-67.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14, 15, 43, 47, 52, 55, 56, 68 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherf et al. (US 5,744,320; cited in the IDS filed 9/17/04) in view of Hawkins et al. (WO 01/96862).

The disclosure by Sherf is discussed *supra*.

Sherf does not disclose the method or kit wherein the first enzyme-mediated reaction is quenched with a nonionic detergent that is not Tween®20 or Triton®X-100.

Hawkins discloses that Tween®20 and Tergitol NP-9 are detergents that have similar effects on auto-luminescence of coelentraine (p. 22, lines 5-15).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute Tergitol NP-9 for Tween®20 in the method or kit wherein the first enzyme-mediated reaction is quenched with a nonionic detergent taught by Sherf. The ordinary artisan would have been motivated to do so because Hawkins teaches that Tween®20 and Tergitol NP-9 are detergents that have similar effects on auto-luminescence of coelentraine. Hence, the ordinary artisan would have had a reasonable expectation that a nonionic detergent such as Tergitol NP-9

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would behave in a manner similar to Tween®20 in the method or kit wherein the first enzyme-mediated reaction is quenched with a nonionic detergent taught by Sherf.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 6-8, 12, 13, 22-24, 32-36, 38-42, 44, 49-51, 54 and 65-67 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 44 and 54 of U.S. Patent No. 5,744,320. Although the conflicting claims are not identical, they are not patentably distinct from each other because the Sherf patent, claim 44 (which depends from claims 26 and 1) recites (a) initiating a first enzyme-mediated luminescence reaction can be mediated by *Renilla reniformis* luciferase; (b) quantifying the luminescence energy from the first reaction; (c) adding a quench-and-activate solution to quench the luminescence energy produced by the first reaction and simultaneously initiating the second enzyme-mediated reaction that is distinct from the first enzyme-mediated reaction wherein the luciferase is from *Photinus pyralis*

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(firefly); and (d) quantifying the luminescence energy produced by the *Photinus pyralis* luciferase.

Thus, claim 44 recites the elected species wherein the first reaction is mediated by a *Renilla reniformis* luciferase and second reaction is mediated by a *Photinus pyralis* luciferase. Sherf defines selective quenching agents for *Renilla* luciferase luminescence in Table 3, wherein Tween®20 and Triton®X-100 are nonionic detergents which meets the elected specie for a selective sequestering agent that is a nonionic detergent.

According to the MPEP 804, the specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in Vogel recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court, one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

Claim 54 of '320 recited the kit elements for a dual reporter assay wherein the first and second luciferase enzymes are selected from the group consociating of beetle luciferase and

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coelenterate luciferins (e.g., *Photinus pyralis* and *Renilla reniformis*, respectively). This group of two possible luciferases for either the first or second enzyme of the claimed dual reporter assay kit is a small genus from which the ordinary artisan could easily select *Renilla reniformis* as the first enzyme for the assay kit. Claim 54 further names nonionic detergents such as Tween®20 and Triton®X-100 which selectively quench *Renilla reniformis* luciferase.

Claims 14, 15, 43, 47, 52, 55, 56, 68 and 69 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 44 and 54 of U.S. Patent No. 5,744,320 in view of Hawkins et al. (WO 01/96862).

The recitations of claims 44 and 54 of the '320 patent is discussed *supra*.

The '320 patent does not claim the method or kit wherein the first enzyme-mediated reaction is quenched with a nonionic detergent that is not Tween®20 or Triton®X-100.

Hawkins discloses that Tween®20 and Tergitol NP-9 are detergents that have similar effects on auto-luminescence of coelenterazine (p. 22, lines 5-15).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute Tergitol NP-9 for Tween®20 in the claimed method or kit of the '320 patent wherein the first enzyme-mediated reaction is quenched with a nonionic detergent. The ordinary artisan would have been motivated to do so because Hawkins teaches that Tween®20 and Tergitol NP-9 are detergents that have similar effects on auto-luminescence of coelenterazine. Hence, the ordinary artisan would have had a reasonable expectation that a nonionic detergent such as Tergitol NP-9 would behave in a manner similar to Tween®20 in the method or kit wherein the first enzyme-mediated reaction is quenched with a nonionic detergent as claimed in the '320 patent.

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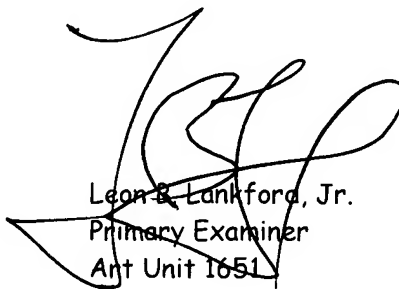
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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